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INCOMPATIBILITY AND SOME OF ITS LESSONS.

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INCOMPATIBILITY AND SOME OF ITS LESSONS.

INCOMPATIBILITY has been variously defined by writers; and I propose to define it as “any unintentional change which notably interferes with the elegance, usefulness, or safety of a prescription.” The subject of so-called therapeutical incompatibility is not included in this definition; for it belongs to a different sphere, and its principles are taught by the science of pharmacology.

Of the other two departments of incompatibility, viz. pharmaceutical, or physical, and chemical, the former will be only briefly dealt with; and my observations will chiefly refer to the chemical aspects of prescribing from a practical and everyday point of view.

Even with this limitation the subject of incompatibility is a broad and almost endless one.

For the number of possible combinations is infinite, and no rules can provide against all possible or even likely cases. Moreover, new drugs bring with them new problems; and some of the recent complex synthetic preparations, e.g. antipyrin, do not readily lend themselves to general rules, and often have a number of special incompatibilities.

PHARMACEUTICAL INCOMPATIBILITY.

The most common cases fall under these heads:—

(1.) Immiscibility, and Insolubility.

For example, glycerin, although it is the organic base of fixed oils (fats), does not intermix with them.

Fats, resins, oleo-resins, hydrocarbons, and volatile (essential) oils are almost insoluble in, or are immiscible with, water, and are

therefore precipitated by water from their alcoholic or ethereal solutions. To render them miscible with water they must be emulsified by some chemical (alkalies) or physical (gum : sugars) means.

R Bals. Copaibæ, ʒij
 Ac. Sulphur. arom., ʒi
 Infus. Rosæ, ad ʒviiij
 M. An impossible feat.

Lanolin is the only fat with which a considerable amount of water can be mechanically incorporated by trituration.

But fixed oils (fats) and volatile (essential) oils are mutually soluble, one in the other, and can be mixed in almost any proportion, e.g. Ol. tereb. and Ol. olivæ; camphor and olive (sweet) oil.

Gums are insoluble in alcohol: hence, mucilage of gum arabic is incompatible with *strong* alcohol.

R Tinct. Cannabis Ind.
 Mucil. Acaciæ, āā ʒss
 M. ʒi to be taken at night.

Gum arabic gelatinizes with ferric salts, lead *sub*acetate, bismuth subnitrate, and borax. Carbolic acid (*not* creosote) gelatinizes with collodion.

The following prescription is wrong:—

R Ac. Carbol., ʒi
 Collodion, ʒvii
 M. Apply with a camel's-hair brush.

The mixture forms a solid mass.

(2.) Deficiency of solvent:—

R Pot. Chloratis, ʒiv
 Aquæ, ʒiiij
 M. Pot. Chlorate requires 16 parts of water for solution.
 R Ac. Carbol., ʒiss
 Aquæ, ad ʒi
 M. Use with a camels-hair brush.

An improper and dangerous prescription. A layer of liquefied carbolic acid (a liquid hydrate) will lie at the bottom of the bottle.

The strongest possible aqueous solution of pure phenol is about 1 in 12, but it is safer not to prescribe a solution stronger than 5 per cent.

Glyc. ac. carbol. (1 in 5) mixes in all proportions with water without separation of phenol. In this way, strong aqueous solutions of phenol are procurable: often a great advantage.

(3.) Undesirable alterations in colour, consistence, or bulk:

E.g. Pills should not be too hard, too soft, or too large.

Unless the prescriber is an expert pharmacist, it is usually wiser to leave the choice of a pill excipient to the dispenser.

Deliquescent substances should never be prescribed in powder form, or in cachets; e.g.: Pot. Acetas. Red Roses (Infusion or Confection) are turned green by alkalies or by magnesia, and by subacetate of lead.

(4.) Interaction of two dry solids in the absence of added water or other liquid.

Two cases occur in this connexion:—

(a) Formation, by trituration, of molecular complexes. These are unstable liquids or pasty mixtures, easily resolved into their components, e.g.:—

Camphor and chloral,
 „ „ menthol,
 „ „ phenols (carbolic acid: resorcin),
 Acetanilide (antifebrin) and antipyrin (phenazone),
 Antipyrin and sodium salicylate,
 Phenacetin, exalgin, or acetanilide with salicylic acid.

R	Chloral hydrate,	gr. 40
	Camphor,	gr. 10
	Syrup of ginger,	℥ii
	Water,	℥iij

M. A teaspoonful 3 times a day.

Impossible to dispense without separation of the camphor, which will float on the top as a soft white solid.

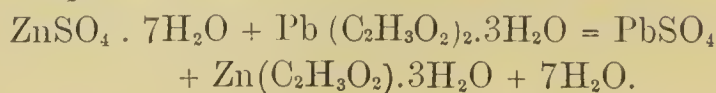
R Chloral Hydr.
 Sulphonal, āā gr. 15
 M. Ft. pulvis.

Forms a soft pasty mass.

R Camphor, gr. i
 Chloral Hydr., gr. vi
 Ext. Hyosey., gr. i
 M. Ft. pil. ij

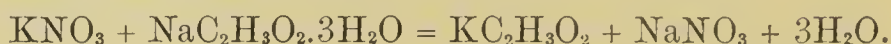
(b) True double decomposition, e.g. :—

Zinc sulphate, or alum, with acetate of lead :



The mass becomes moist when triturated, owing to liberation of some of the water of crystallization.

Similarly, potassium nitrate and sodium acetate :—



Most cases of physical incompatibility can be remedied, or, better still, prevented by paying due attention to :—

- (a) The order of mixing the ingredients.
- (b) By alterations in the solvents, or, by protective agents (gum : sugar : glycerin).
- (c) By emulsifying or suspending the insoluble body with gum or syrup.

CHEMICAL INCOMPATIBILITY.

We may accept as a primary rule :—*Have as little chemical action as is possible take place among the ingredients of a prescription, unless such is clearly ordered or intended.*

This rule holds good, although it must be admitted that some chemical precipitates may be dissolved in the stomach with comparative facility. If only on the ground of elegance, such precipitates should be, and can readily be, avoided.

It is worth while to observe that chemical change between two substances can sometimes be much retarded, or even prevented,

by forming a *dilute* solution of one of them in a mucilaginous or syrupy liquid before adding the other.

The *order of mixing* the ingredients in a prescription is often of material importance, e.g.:—

Corrosive sublimate,	.	.	.	gr. ss
Ammon. carbon.				
Potass. iodid.,	.	.	.	āā gr. v
Aquæ,	.	.	.	ad 3i

M.

The ammon. carb. would precipitate with the HgCl_2 if directly added to it.

But if the HgCl_2 and KI be first dissolved and the ammon. carb. be added to this solution, no precipitation occurs (Scoville).

Again, mix (in order as named):—

Corrosive sublimate,	.	.	.	gr. iii
Water,	.	.	.	3ij
Mucilage,	.	.	.	3i
Lime-water,	.	.	.	3ij

Contrast with the effect of adding the lime-water to the corrosive sublimate *before* the addition of mucilage.

Tr. ferri perchlor.,	.	.	.	℥15
Syrupi,	.	.	.	3i
Aquæ,	.	.	.	3v
M. et adde				
Spir. ammon. arom.	.	.	.	3ij

Most of the iron remains in solution. But if the spirit of ammonia were added *before* the syrup, all, or nearly all, the iron would be precipitated as ferric hydroxide.

The classes of chemical incompatibilities are grouped under two headings, viz.:—

I. **Homogeneous systems**, i.e. unattended with any visible *change of form*. There may be colour alteration.

II. **Heterogeneous systems**, i.e. attended with a visible *change of form*, viz. the production of either a gas (or volatile substance), or a precipitate.

The formation of a gas or volatile substance naturally is favoured by a rise of temperature. The chief gas concerned in incompatibilities is carbon dioxide; more rarely, H_2S , or SO_2 . But since precipitates, i.e. insoluble compounds, formed at ordinary temperatures, afford by far the largest class of chemical incompatibilities, it is very essential to acquire a clear knowledge of the ordinary rules of solubility. This will enable us to understand and to avoid most of the common pitfalls.

The important elements in the B.P. number thirty-two, and of these about twenty are concerned in incompatibilities.

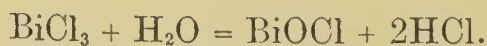
Generally speaking, whenever an insoluble body can be produced by the mutual inter-action of any two bodies it will be formed, because a chemical reaction tends to the production of the most stable body possible under the given conditions. The ordinary tables and charts of qualitative analysis are based upon the rules of solubility. For example, Group I., viz. metals precipitated by hydrochloric acid, is only another way of looking at Rule 5, and so on for the other groups, e.g. precipitation of the heavy metals as sulphides by H_2S . (Rule 1.)

General principles:—

(a) Water, which is rich in oxygen ($\frac{8}{9}$ by weight), dissolves most inorganic salts rich in oxygen, and almost all haloid salts (chlorides, bromides, iodides).

(b) Organic substances poor in, or wanting in, oxygen (hydrocarbons, vaselin, guttapercha, caoutchouc, fats, volatile oils, resins) are usually more soluble in bodies relatively poor or deficient in oxygen, e.g. alcohol, ether, chloroform, petroleum oils, benzene, oil of turpentine.

(c) Some salts, theoretically soluble, are decomposed by water (hydrolysis) and yield a ppt. of basic salt, oxychloride, &c., e.g. BiCl_3 , SbCl_3 , ZnCl_2 .



RULES FOR SOLUBILITY IN WATER.*

(1) All metallic **oxides**, **hydroxides**, and **sulphides** are insoluble, except those of the alkalis (K, Na, NH_4 , L), and alkaline earths (Ba, Sr, Ca).

Lime, $\text{Ca}(\text{OH})_2$, is sparingly soluble, 1 in 800; vegetable bases, (alkaloids) are mostly insoluble, and do not form carbonates; hence they are usually precipitated from their salts by soluble hydroxides or carbonates. Sulphides are easily decomposed by acids, and yield H_2S . H_2O_2 pps. CaO_2 from lime-water.

(2) All normal† (neutral) metallic **nitrates**,‡ **chlorates**, and **acetates** are soluble; silver and mercurous acetates, sparingly.

Quinine acetate is insoluble. Some basic (oxy) acetates and nitrates are insoluble, e.g. bismuth subnitrates, BiONO_3 .

Normal bismuth nitrate, $\text{Bi}(\text{NO}_3)_3$ is decomposed by water, but is stable for a time in solution in glycerine.

Subacetate of lead precipitates gum, most vegetable colouring matters, and many organic acids. **Nitrites** are mostly soluble (except AgNO_2), but are unstable.

(3) All normal **phosphates**, **arsenates**, **arsenites**, **carbonates**, and **borates** are insoluble, except those of the alkalis. Lithium carbonate and phosphate are sparingly soluble.

The acid (bi) salts are often soluble, e.g. of Ca and Mg (fluid magnesia, superphosphate of Ca).

The phosphates of Fe and Ca, arsenate of Fe, and carbonates of Fe, Ca, Zn, Pb, and Mg are the insoluble salts of this group in the B.P. A little free acid, even acetic, will keep in solution, or redissolve many insoluble phosphates. FePO_4 is insoluble in acetic acid.

* Probably no substance is absolutely insoluble in water.

† A *normal* salt is one in which the acidic hydrogen is exactly replaced by the equivalent amount of basic or metallic radical. Such a salt may be indifferent to litmus, or may redden (CuSO_4) or blue (Na_2CO_3) the test-paper. Hence the synonym "neutral" is ambiguous, and the term should be discarded in this connexion.

‡ Urea nitrate is readily soluble in water but is insoluble in strong colourless HNO_3 , a fact often witnessed in the clinical testing of urine.

(4) All normal **sulphates** are soluble except those of Ba, Sr, Pb. BaSO_4 is the least soluble of these three sulphates. Hence, a soluble salt of Ba (BaCl_2) is the common and delicate test for the SO_4 ion. Failing Ba, a solution of lead acetate will answer. Radium sulphate is even less soluble than BaSO_4 . PbSO_4 is the only one of importance in pharmacy. Calcium, silver, and mercurous sulphates are sparingly soluble.

Sulphites are mostly insoluble, except those of alkalies.

(5) All **chlorides** and **bromides** are soluble except AgCl , AgBr , NH_2HgCl (white ppt.), Hg_2Cl_2 (calomel), Hg_2Br_2 , and Cu_2Cl_2 . Lead chloride and bromide are sparingly soluble.

Some bromides and chlorides, e.g. SbCl_3 , BiCl_3 , and ZnCl_2 , are decomposed by water (hydrolysis), and an insoluble oxychloride or bromide is precipitated.

Liq. bismuthi is incompatible with Ac. hydrochlor. dil. or Ac. nitr. hydr. dil., and it should be prescribed in neutral or alkaline solutions.

(6) Most **iodides** are soluble, except those of lead, mercury, silver, bismuth, and Cu_2I_2 .

HgI_2 (red) dissolves easily in solution of KI, forming a colourless double salt ($\text{HgI}_2 \cdot 2\text{KI}$).

(7) Most **oxalates**, except those of alkalies and of Mg, are insoluble, e.g. calcium and cerium. Hence, magnesia cannot be substituted for lime as an antidote to oxalic acid, because soluble oxalates are toxic.

From the above rules it will be seen that *nearly all salts of the alkali radicals are soluble*, and hence alkalies may generally be neutralized by acids, and their salts may be prescribed in any combinations, *inter se*, without fear of precipitation, e.g. $\text{KI} + \text{Na}_2\text{SO}_4$. Acid tartrates of potassium or ammonium, acid oxalate of sodium, and picrate of potassium are very sparingly soluble. Acid urate of Na forms the "chalk-stones" of gout.

On the other hand, the majority of the mercurous, lead, and silver salts are insoluble, except the acetates and nitrates.

Salts of the *same acid* radical do not, as a rule, mutually decompose each other. They often combine to form double salts,

e.g. the group of alums, and Mayer's solution ($\text{HgI}_2, 2\text{KI}$). Magnesium sulphate should not be prescribed along with Rochelle salt (soda tartarata), for, after some time, magnesium tartrate will be precipitated. Potassium iodide and potassium chlorate may interact and form irritant potassium iodate.

Alcohol.—In regard to alcohol as a solvent it is not possible to formulate exact rules, but it may be useful to observe that most acetates, benzoates, nitrates, salicylates, valerianates, and halogen salts (chlorides, bromides, and iodides) are soluble in alcohol, while most other salts are insoluble, except those which are deliquescent (Scoville). Metallic sulphates, nitrates, and phosphates are usually insoluble in alcohol. Hence the ppt. formed when strong alcohol is floated on urine, i.e. phosphates and sulphates.

Solution of Magnes. sulph. (1 in 2),	.	$\bar{3}_{ss}$
Sp. æth. nitrosi,	.	$\bar{3}_{ss}$

This becomes solid after a few minutes.

Castor oil and croton oil are the most soluble in alcohol of the fixed oils.

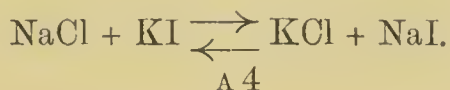
Glycerine.—Its solvent powers lie between those of alcohol and water. It decomposes borax, and liberates boric acid.

HOMOGENEOUS SYSTEMS.

By this term is meant cases where all the products of reaction are soluble, and nothing, either gaseous or solid, visibly separates out from the sphere of action.

It must not, however, be supposed that when two soluble salts in solution are mixed, and nothing *appears* to happen, there is really no change, e.g. $\text{NaCl} + \text{KI}$.

On the contrary, there are sound reasons for believing that, in all such cases, double decomposition actually occurs, and that instead of only two salts we really have four salts in solution. That is to say, the reaction is reversible, as expressed by the symbols,



In other words, we have in solution (*a*) a certain amount of two newly-formed salts, and (*b*) a certain amount of the two original salts formed by re-composition of the products of reaction. These four salts are balanced against each other in a state of mobile or dynamic, *not* static, equilibrium.

So that a chemical equation should usually be interpreted not only from left to right, but also in the reverse direction from right to left.

The interchange goes on until the opposing reactions have attained equal and opposite velocities, when finally the "peace of dynamic equilibrium" is established.

In some cases, the progress of such a change is obviously shown by colour change, e.g. when a soluble alkaline acetate is added to a soluble ferric salt.

The state of equilibrium and the reaction velocity are dependent, not only upon the active masses of the reacting bodies, but further upon a number of factors, e.g. temperature, pressure, electrical conditions, and illumination, which collectively may be regarded as being associated with the introduction of energy *into* or the abstraction of energy *from* the system.

Of these factors, temperature is the most influential, and experiment shows that most reactions double or treble their velocity for a rise of 10° in temperature. Explosive reactions are, of course, non-reversible.

(1) **Acids and Bases**, in the free state.

(*a*) Generally speaking, these bodies are chemically and therapeutically incompatible; and it is inadmissible to prescribe, e.g.* lactic acid with lime-water. This has been prescribed as a gargle.

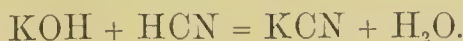
Similarly, Lin. tereb. acet. with Liq. Ammonię, or Lin. camph. ammon.; Ac. nitro-hyd. dil. with Spir. ammon. aromat.

(*b*) But if the resulting salt be soluble and poisonous, the toxic action persists in spite of chemical neutralization, e.g. oxalic acid

* The illustrative examples are selected from actual prescriptions. Some of the examples are culled from Scoville's *Art of Compounding*, and from Ruddiman's *Incompatibilities in Prescriptions*, 3rd edit.

and alkalies ("salt of lemon"). Lime-water is the antidote for oxalic acid (Rule 7).

Hydrocyanic acid and alkalies.



The physiological action of KCN substantially agrees with that of HCN.

Alkaline bicarbonates are not decomposed by HCN. This is a favourite and proper combination.

(2) **Halogen compounds**, *i.e.* of Cl, Br, I.

The order of affinity for hydrogen and metals is :



Hence free Cl or Br will liberate iodine from iodides.

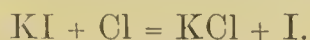
The order of affinity for oxygen combination is :



There is no known oxide of bromine.

Chlorides are the most stable group, and alkaline iodides are more unstable than the corresponding bromides and chlorides. It is important to become familiar with some decompositions of iodide of potassium, *e.g.* :—

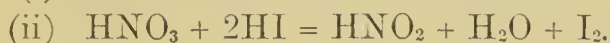
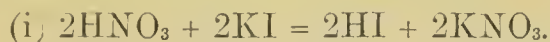
(a) By free Cl or Br (avoiding excess) or by *Ae. nitr. hyd. dil.* :



Free Cl can be detected in chloroform by addition of KI (or CdI_2 , B.P.), and starch mucilage.

(b) By nitric or nitrous acids :

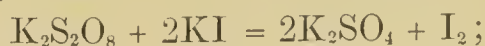
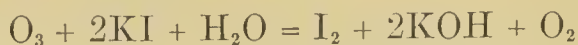
The reaction may go on in at least three stages (Reynolds) :—



It is easy to detect KI in urine by this means.

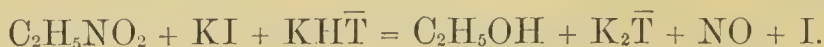
The free iodine is evidenced by starch, or by the rose-red colour imparted to chloroform when agitated with the urine. The test for nitrites in drinking-water is based upon the same principle.

Persulphates, H_2O_2 , or ozone, liberate iodine from KI :



and hence the guaiacum test cannot be applied to the detection of blood in presence of KI.* Slow decomposition occurs between KI and Bism. subnitras. A common change is with Sp. ætheris nitrosi, which frequently contains free acid, or with Liq. ethyl nitritis, or amyl nitrite. These combinations are better avoided, even after neutralization with alkaline bicarbonate.

Acid salts in conjunction with nitrites favour decomposition :



Paraldehyde may liberate iodine from KI.

(c) *inorganic* ferric salts—



This is an unsuitable and very irritant combination, owing to the free iodine. The undesirable change does not occur with ferric acetate, nor with the “scale preparations” of iron. Therefore, Ferri et amm. citr. or Ferrum Tartar. and KI are quite compatible. KI is incompatible with Ferri et Quin. citr.

Alkaline bromides are not decomposed by iron salts, unless the solution be very acid, and concentrated.

KI can, of course, be suitably given along with Syr. ferri iod. or any ferrous salt.

(d) Observe the action of KI upon copper sulphate. Weak solutions form no ppt. at once. With stronger solutions iodine is liberated and cuprous iodide ppd. :



* Pot. iodidi, gr. ʒ2

Vin. colch., ℥ ʒ2

Æth. ozonic (Robbins), ʒ vi

Syr. aurantii, ʒ v

Aquæ, ad ʒ vi

M.

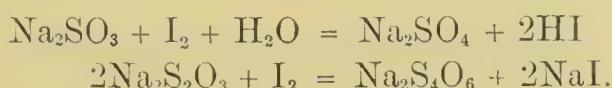
Upon one occasion a yellow crystalline ppt. was formed; and upon another, the bottle burst with explosion. (*Ph. J.*, 3rd Ser., xii., 432.)

(e) Note the action of free Cl, Br, or I respectively upon Liq. ammoniæ (*see* Heterogeneous Systems).

(f) "Colourless" tincture of iodine, so-called. This is an impossibility, for free iodine always forms a coloured solution.

The means adopted for decolorising (!) depend upon formation of either :

(i) A colourless salt, e.g. by action of the fixed alkalies ; sulphites ; thiosulphate (hyposulphite) of sodium :



Upon *aqueous* solutions of iodine, viz. Liq. iodi fortis, B.P. the action of potash (or soda) is :



Similarly with bromine and chlorine, when heated. This reaction is the basis of the B.P. processes for preparing KI and KBr. Hypo-iodite and iodide are always formed at first: then the hypo-iodite turns into iodate and iodite (Taylor).

With *alcoholic* solutions of iodine, e.g. Tinctura iodi, upon addition of alkalies, iodoform, CHI_3 , is formed and precipitated as a fine yellow powder (hexagonal crystals). This is Lieben's test for alcohol, and is used in B.P. for detection of chloral-alcoholate in chloral :—



(ii) An organic substitution compound, e.g. with tannin or with phenols (carbolic acid ; resorcin), e.g. Draper's Tincture of iodine.

(g) Note particularly the incompatibility between Syr. ferri iodidi and potassium chlorate.

This requires a little time for its development, and so may be overlooked.

The following prescription was ordered for a child :—

Pot. chloratis,	℥ii
Syr. ferri iod.,	ʒiv
Syr. simpl.,	ʒiv
Sp. chlorof.,	mxx
Aquæ,	ad ʒii

The mixture gradually darkened, and in a few hours deposited iodine in abundance. In this condition it was given to the child, with the result that serious symptoms set in, terminating fatally. The dispenser was unjustly blamed by the prescriber.

Neutral Syr. ferri iod. (or in presence of pot. citrate or pot. acetate) is not decomposed; but if, as frequently happens, it contains some free hydriodic acid, the solution becomes yellow, or brown, and iodine is abundantly liberated:



Chloric acid is, possibly, first liberated. Ultimately hydrated ferric oxide may be thrown down, and possibly some irritant potassium iodate may also be formed.

This reaction, then, may also be partly a heterogeneous one. Potassium chlorate is compatible with ferric salts.

(3) Ferric salts and acetates.

The mixture (Basham's mixture) becomes blood-red,* from formation of ferric acetate. Therapeutically, quite admissible and harmless; as is likewise red ferric meconate produced when Tinct. opii is combined with Tinct. ferri perchloridi.

Ferric chloride strikes a deep red with antipyrin, and violet purple with salicylates, and violet with carbolic acid in aqueous solution.

(4) Formation of nitro- and nitroso- compounds.

Resorcin with sp. æth. nit. = dark red.

The solution made from the subjoined formula turned a permanent dark red, and produced severe irritation upon the skin:—

Rx	Hydrarg. perchlor.,	gr. iv
	Resorcin,	5 i
	Spir. chlorof.,	aa 5 ii
	Spir. æth. nitr.,	M.

* According to Mendeléeff, *normal* ferric salts are colourless, or nearly so (e.g. iron-alum, ferric oxalate, ferric phosphate), and the brown or yellow colour is really due to basic ferric salts.

Antipyrin with spir. ætheris nitr. = green.

This reaction (using NaNO_2) is given as a test for phenazone (antipyrin) in B.P. The incompatibility may be avoided by prescribing them in alkaline solution. Liq. Ethyl Nitritis, B.P. is more stable, and should always be prescribed in preference to Spir. Aeth. Nitr.

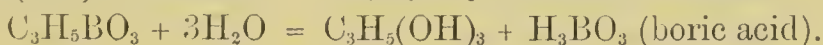
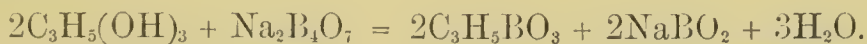
Sodium salicylate (or Bism. salicylate) with spir. æth. nitr. = red.

Bismuth subnitrate gives a red compound with salicylic acid or sodium salicylate. Acetanilide (antifebrin) *slowly* develops a yellow or red colour with sp. æth. nitr.

It is better to avoid any of these combinations; and nitrites should always be prescribed in as simple a form as possible.

(5) Glycerin and borax.

Borax is decomposed by polyhydric alcohols, e.g. glycerin, glucose, and honey (mel boracis), not by sucrose. In *aqueous* solution borax reacts alkaline; but Glycerinum boracis reacts acid, and contains free boric acid, and therefore is incompatible with carbonates :



Borax forms a tenacious jelly with mucilage of gum arabic. Prevented by syrup or glycerin.

HETEROGENEOUS SYSTEMS.

i.e. either a precipitate formed or a gas liberated.

Sometimes an intentional incompatibility is committed, e.g. all effervescing draughts : seidlitz powders ; sodii. phosph. efferv. B.P. ; sodii sulph. efferv., B.P. ; sodii citro-tart. efferv., B.P. ; lotio nigra (black wash), and lotio flava (yellow wash).

Some incompatibilities are trivial and comparatively unimportant, e.g. vegetable astringents (tannic and gallic acids) with iron salts ; lead salts and opiate solutions (meconate of lead) ; ferric chloride and tincture of opium (ferric meconate).

In very dilute solutions, e.g. of HgCl_2 , it is obvious that precipitations may not occur which would happen in stronger solutions.

Of the more important unintentional changes which should, as a rule, be avoided, we will notice :—

(1) Action of halogens upon Liq. ammoniæ.

The reaction between the halogens and the fixed alkalies has been already referred to.

With ammonia the case is different.

(a) Free Cl or Br liberates nitrogen gas, and the effervescent solution is colourless :

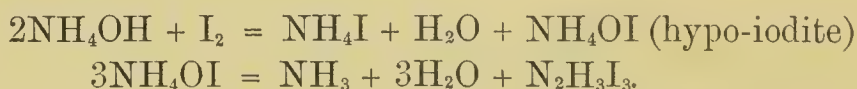


(b) A more important reaction occurs with iodine.

When Liq. ammoniæ (or Lin. camph. ammoniatum) is added to Tinct. iodi (or Liquor iodi), the colour of the iodine is discharged, and a black precipitate forms, the so-called iodide of nitrogen.

This is a most unstable substance, and when dry very explosive. Dangerous accidents have occurred through ignorance or carelessness in dealing with it, after collection on a filter. The black precipitate is an iodine derivative of ammonia, and its formula is usually given as NHI_2 or NI_3 . But according to Chattaway and Orton, the true formula is $\text{N}_2\text{H}_3\text{I}_3$ (NH_3 , NI_3), and they have obtained it in well-defined copper-coloured crystals.

The theory of its formation is :



Iodide of nitrogen is also liable to be formed when alcoholic solution of iodine is left in contact with white precipitate.

Iodide of nitrogen is analogous in composition to silver fulminate, NAg_3 or NHAg_2 , but not to fulminate of mercury, $\text{C}_2\text{Hg}(\text{NO}_2)\text{N}$, which is a derivative from the nitro-acid $\text{C}_2\text{H}_2(\text{NO}_3)\text{N}$.

(2) Liberation of an acid gas (CO_2 or H_2S).

Carbonates are decomposed by :—

(a) Free acids, except HCN and H_2S : Glycer., Boracis.

Examples of such stupid combinations are:—Ac. sulphuric dil. with Mist. cretæ; Nitromuriatic acid with aromatic spirit of ammonia; oxymel, or Syrup of squill (acetic acid), with carbonates, bicarbonates, Spir. ammoniæ aromat.*

(b) Acid salts, e.g. cream of tartar, KHT.

If grey powder (hyd. c. cretâ) be rubbed up with conf. sulphuris (KHT), the pasty mass slowly swells and becomes frothy from evolution of CO_2 . Some HgS is also formed.



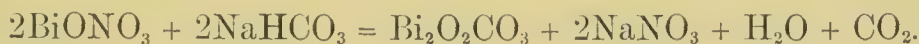
(c) Basic salts, e.g. Bism. subnitrates.

This slowly decomposes alkaline bicarbonates, especially if gently warmed:—

Sodæ bicarb.,	3 ij
Bism. alb.,	3 ij
Sp. Ammon. arom.,	3 ij
Sp. chlorof.,	3 i
Aquæ,	ad 3viii

M.

After the bottle had been put aside for an hour it burst.



Bismuth carbonate should be substituted for the nitrate.

If bismuth subnitrate be added to chalk mixture, CO_2 will be slowly evolved.

(d) Double citrates, e.g. scale preparations of iron, viz. ferri et amm. citr.; ferri et quin. citr.

The following prescription could not be dispensed without some effervescence:—

Pot. bicarb.,	3 ij
Pot. iodidi,	3 i
Ferri ammon. citr.,	3 ij
Aquæ aurantii,	ad 3iii

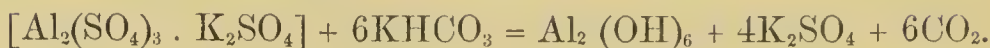
M.

* Several official preparations contain free acid: viz. Acetum scillæ; Infusum rosæ acidum; ~~Liq. tart. acetatis~~; Syr. calcis lactophosph.; Syr. ferri phosph.; Syr. ferri phosph. c. quin. et strychn.; Syr. limonis; Syr. scillæ.

(e) Double sulphates, e.g. alum—

R	Glyc. aluminis,	3i
	Pot. bicarb.,	3 iss
	Pot. chloratis,	3 i
	Aquæ,	ad 3iv
M.	Ft. gargarisma.						

This froths up at once, and pps. aluminum hydroxide.



Sulphides, e.g. CaS, are decomposed by acids, and H₂S liberated.

Potassium chlorate and KMnO₄ react with strong HCl, and Cl gas is set free.

H₂O₂ and KMnO₄ evolve oxygen.

With H₂SO₄, Cl₂O₄ is liberated from KClO₃.

(3) Liberation of an insoluble acid.

Free benzoic and salicylic acids are sparingly soluble. Add a mineral acid (HCl. HBr) (H₂SO₄), e.g. Infus. rosæ acidum, to solution of ammonium benzoate or sodium salicylate, and note the abundant crystalline precipitate. Syr. limonis also pps. Sod. salicylate.

Neither acetic nor boric acid will cause precipitation.

Some glucosides, e.g. glycyrrhizin, are precipitated from their solutions, viz. Ext. glycyrrh. liq., by mineral acids, and an unsightly brown mass produced.

(4) Mercurials.

The following points should be noted:—

(i) Mercurous compounds are more unstable than mercuric compounds, e.g. green iodide of mercury, Hg₂I₂, which has been rejected from the B.P. owing to its instability, and partial change into HgI₂.

(ii) Mercuric (per) compounds sometimes assume allotropic forms, e.g.:

Mercuric oxide, HgO, red (red precipitate) and yellow forms

(both official). The yellow form is in a finer state of subdivision, and hence is preferred for eye ointments.

Mercuric iodide, HgI_2 (red; yellow form when heated).

(iii) Mercuric compounds readily form double salts, e.g. Donovan's solution (Liq. arsen. et hydr. iod.).

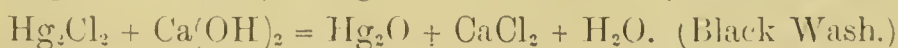
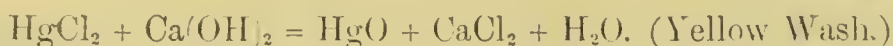
This solution should not be prescribed along with Liq. Hydrarg. ✓
Perchlor.; because HgI_2 is ppd.

Lister's zinc-mercuric cyanide, $\text{HgCy}_2 \cdot 4\text{ZnCy}_2$; (cyanide gauze).

Mayer's reagent for alkaloids $\text{HgI}_2, 2\text{KI}$; Sal alembroth $\text{HgCl}_2, 2\text{NH}_4\text{Cl}$.

(iv) All mercurous (snb) compounds are insoluble, except HgNO_3 .

Both oxides of mercury are insoluble, and intentional incompatibility is exemplified in Lotio hydrarg. flava, and in Lot. hydrarg. nigra formed by action of lime-water on the corresponding chlorides:—



Liq. potassæ and Liq. sodæ and their carbonates react similarly to lime-water.

R	Hydrarg. perchlor.,	gr. i
	Liq. Fowler,	ʒ iss
	Potass. iodidi,	ʒ i
	Liq. peptici,	ʒ ij
	Infus. Cinch.,	ad ʒ viii

M.

About as bad a prescription as could be devised.

Mayer's reagent is formed and pps. the alkaloids of the Cinchona bark.

To prescribe corrosive sublimate with arsenic use Liq. arsen. hydrochlor., and not Fowler's solution, which is alkaline (K_2CO_3).

A solution of HgCl_2 in glycerine is not precipitated by Liq. ✓
potassæ in the cold.

Ammonia acts quite differently on mercurial salts.

With corrosive sublimate it forms "white precipitate" (Hydrarg. ammon., B.P.).

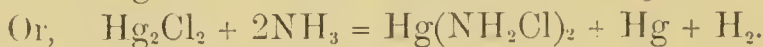


R	Hydrargyri Perchloridi,	.	.	.	gr. x
	Ac. Tannici,	.	.	.	gr. xx
	Liq. Ammon. Fort.,	.	.	.	℥iv
	Aquæ,	.	.	.	ad ℥x

M. Ft. lotio.

Wrong from every point of view.

With calomel, "black precipitate" is formed (not official).



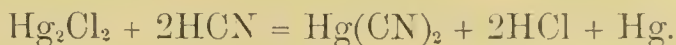
Ammoniae carbonatis,	.	.	.	℥i
Hydrarg. chlor. mitis,	.	.	.	gr. xii

M. Ft. capsulae, No. viij

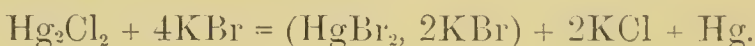
On triturating these two substances together the mixture becomes black.

Borax added to HgCl_2 precipitates red oxychloride of mercury.

Calomel is converted into mercuric salt by KCN and even by HCN, and turns black from liberation of metallic mercury:—



Calomel is decomposed and blackened by bromide of potassium in presence of a trace of moisture.



This is a dangerous incompatibility, and these two salts should never be prescribed together, for a poisonous mercuric salt is formed.

The following prescription was written for a child (result to child not stated):—

Potass. brom.,	gr. x
Calomel,	gr. iii

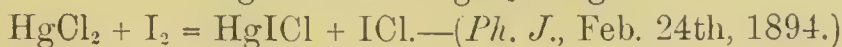
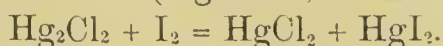
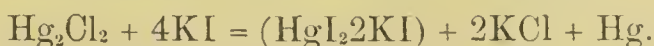
M. Mitte tales iii.

(*Ph. J.*, Feb. 24th, 1894.)

Calomel is decomposed by pure iodide of potassium and blackened, and yellow mercurous iodide is also formed. Violent

irritation of the eye from formation of HgI_2 , may arise from the application of Pagenstecher's ointment (yellow HgO) or of calomel to the eye of a patient who is taking an iodide, e.g. cod liver oil and syrup of iodide of iron internally. Syrup of phosphate of iron should be prescribed. If calomel be added to the saliva of a patient who is taking KI , a yellow ppt. of mercurous iodide will appear.

Tincture of iodine acts upon calomel in a somewhat complex fashion, with precipitation of red iodide of mercury.



This is a dangerous and objectionable reaction.

The following prescription was ordered to be painted on a glandular swelling on the neck:—

Tinct. iodi. $\bar{3}$ i; calomel gr. xx. M.

Calomel, or grey powder, and iodoform left in contact, turn scarlet from formation of HgI_2 . The reaction possibly is:



Corrosive sublimate is, in one sense, incompatible with KI ; and mixed in molecular proportions, red iodide of mercury is precipitated (B.P. process).

But excess of KI quickly forms the colourless solution of double iodide ($\text{HgI}_2 \cdot 2\text{KI}$), so that the favourite combination of, say, 1 gr. HgCl_2 in $\bar{5}$ vi of solution KI (5-10 grains to $\bar{3}$ i) is quite legitimate and therapeutically efficient.

R	Pulv. calcii sulphidi,	.	.	.	gr. xv
	Liq. hydr. bichlor.,	.	.	.	5 vi
	Pot. iodidi,	.	.	.	gr. xl
	Pot. bicarb.,	.	.	.	5 iiss
	Aq. chlorof.,	.	.	.	ad 5 viii
M.					

No ingenuity can render this prescription presentable.

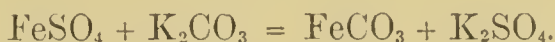
Thoroughly wrong.

(5) **Chalybeates** (Ferrous and Ferric salts).

The following points should be noted:—

The reaction between Syr. ferri iod. and Pot. chloras has been already explained. Potassium chlorate is not incompatible with ferric salts.

Ferrous carbonate is insoluble (Rule 3), and intentional incompatibility is exhibited in Mist. ferri co.; and in Pilula ferri, B.P.



A similar change happens when Blaud's pill comes into contact with water.

Both ferrous and ferric oxides are insoluble (Rule 1).

Therefore, all *inorganic* iron salts are incompatible with alkalies and their carbonates. Ferric carbonate does not exist.

R	Liq. arsenicalis,	℥ iij
	Syr. ferri iodidi,	5 ss
	Aquæ,	ad 5 ss
M.		

Ferrous carbonate is ppd.

To combine suitably perchloride of iron with arsenic use Liq. arsen. hydrochlor., and not Liq. arsenicalis (K_2CO_3); and to prescribe iron in effervescence, add the iron salt to the *acid* bottle, or use a "scale preparation." ("Masked" iron.)

The double salts, Ferri et ammon. citr. and Ferrum tartaratum behave differently, and are not precipitated by alkalies in the cold. Hence, this combination—a common one—is justifiable. Ferri et quin. citr. is less stable, and gives a reddish brown precipitate of ferric hydroxide with Liq. potassæ and a white precipitate of quinine with Liq. ammoniæ. Syrup, glycerine, or mucilage retard or inhibit the precipitation of iron salts by alkalies, but ferric chloride and mucilage, unless well diluted, form a tenacious brown jelly. Glycerine or sugar hinders the oxidation of ferrous salts; e.g. Syr. ferri iodidi.

(6) Insoluble sulphates (Rule 4).

Of these lead sulphate is the only one of importance in pharmacy.

It is inexcusable to prescribe together soluble lead salts (nitrate : acetates) with the "SO₄" ion; e.g. Ac. sulphuric dil., or Ac. sulphuric aromat.: alun,* or zinc sulphate. The last combination is sometimes defended upon the singular ground that insoluble lead sulphate is the really important ingredient (!). Zinc acetate should be substituted for the sulphate. As already explained, either alun or zinc sulphate rubbed up in the dry state, with sugar of lead, undergoes double decomposition.

Liq. plumbi subacet., in excess, gives a *green* precipitate with Infus. rosæ acidum (H₂SO₄), owing to a secondary action of the basic lead salt upon the colouring matter of the red rose. Lead subacetate pps. mucilage of gum arabic.

Liq. Plumbi subacet.,	3 ss
Mucil. acaciæ,	3i
Aq. destill.,	ad 3iv
M. Ft. lotio.	

A solid gelatinous mass is formed.

The apparently isomeric sulphocarbolates of zinc and sodium do not react as sulphates, and are compatible with lead salts, because they do not contain the diad ion "SO₄." They are really salts of monobasic sulphonic acid, SO₂ $\frac{\text{OH}}{\text{H}}$, and are therefore phenol-sulphonates;

i.e. Na·OH·C₆H₄SO₃ and Zn (OH·C₆H₄·SO₃)₂.

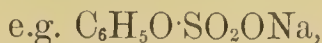
In B.P. 1885 the formula was inadequately presented as—



* The following stupid prescription was ordered:—

Plumbi acet.	
Alum. exsic. āā,	5i
Ac. tannici,	5i
Aquæ,	3i
M. A tablespoonful in a pint of tepid water as a lotion.	

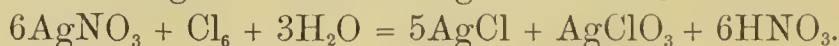
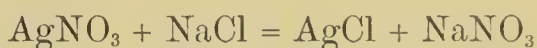
Sulphocarbolates should not be confounded with the isomeric true phenol-sulphates (ethereal sulphates);



which are decomposed by boiling with HCl, phenol and an ordinary sulphate being produced. Ethereal sulphates occur in urine after the administration of phenol.

(7) Insoluble Chlorides (Rule 5).

The most important salt in relation to pharmacy is AgCl, produced whenever AgNO₃ comes into contact with the dissociated chlorine ion.



Hence—

(a) The necessity for using pure distilled water, free from chlorides, in preparing solutions of AgNO₃.

(b) The utility of NaCl as a means of neutralizing any excess of AgNO₃ when locally applied to the eye or elsewhere; and as an antidote in poisoning.

(c) The impropriety of prescribing AgNO₃ along with soluble chlorides or hydrochlorides, e.g. hydrochlorides of cocain or morphine. The nitrates of the alkaloids would be admissible.

Silver nitrate,	1·5 gm.
Sodium chloride,	0·6 gm.
Water,	200 cc.

M.

A stupid combination.

When chlorine is not in the ionic or dissociated state, but is a permanent member of a compound group or radical, as, e.g., in chloral and chloroform, AgNO₃ does not form a precipitate of AgCl, and is therefore used as a test for free chlorides in either of these compounds.*

Stains on the skin resulting from AgNO₃, are best removed by potassium cyanide, which forms a soluble double cyanide.

* For an exposition of the doctrine of ionization the reader is referred to any recent work on physical chemistry.

Insoluble Iodides.

Hg $\frac{1}{2}$

Hg 1

Pb $\frac{1}{2}$.

(8) Insoluble sulphides.

The sulphides of all the heavy metals are insoluble (Rule 1), and some of them are of distinctive colour, facts of much importance in qualitative analysis.

Most insoluble sulphides are black ; hence—

(a) The black stools passed after the use of preparations of iron (FeS) or of bismuth (Bi_2S_3).

(b) Burton's "blue line" on the gums or cheeks, as a result of chronic lead-poisoning (PbS).

(c) The incompatibility of Bism. subnitrate with Sodii hyposulph. (thiosulphate).

(d) The risk of causing black marks upon the skin if preparations of Hg or Pb are applied along with or followed by sulphur, or by preparations containing it in an unoxidized state.

I have seen a patient's face stippled with black dots (HgS) as the result of a mercurial application followed by a preparation of sulphur. A lad, after taking ichthyol internally for an erythematous eruption of the face, used a "lactate of lead" lotion,* and speedily the pores of the skin were blackened owing to the elimination of some sulphur through the skin (R. Crocker).

Zinc sulphide is white ; and accordingly preparations of zinc, if ordered in conjunction with sulphur or sulphides, will not cause discoloration on the skin.

Potassa sulphurata (liver of sulphur) and zinc sulphate are sometimes combined in a lotion, and white zinc sulphide will be precipitated.

(9) Insoluble tannates.

Tannic acid precipitates most of the heavy elements, and is incompatible, e.g. with tartar emetic (vinum antimon.). Tartar emetic is a salt very readily decomposed either by weak acids or alkalies.

Tannic acid also precipitates gelatin, starch, albumen, and most of the alkaloids.

* The formula given by Crocker for lead lactate (*sic*) is: Solution of subacetate of lead, \mathfrak{z} i, fresh milk, \mathfrak{z} ij. Shake well together in a bottle.

(10) Insoluble Oxides and Bases (Rule 1).

E.g., Yellow Wash: Black Wash (p. 21).

H₂O₂ pps. calcium peroxide, CaO₂, from lime-water. All vegetable bases (alkaloids) are sparingly soluble.

R Liquor calcis, ʒ ij
 Zinci sulphatis, gr. x
 Aquæ, ad ʒi

M.

R Liq. Plumbi Subacet. fort. . . . ℥ vi
 Glycerini, ℥ x
 Liq. calcis, ad ʒi

M. Ft. lotio.

In each case the oxide of the heavy metal will be ppd.

(11) Alkaloids.

In view of the highly poisonous properties of some alkaloids their incompatibilities deserve careful study.

(a) Nearly all alkaloids in the *free state* are sparingly soluble in water (Rule 1), and they do not readily form carbonates. Caffein and codein are soluble in 80 parts of water.

Most of their salts are soluble in water, especially if the water be slightly acidulated; e.g. quinine sulphate.

Solutions of quinine in oxy-acids exhibit blue fluorescence, destroyed by a haloid acid (HBr) or salt (KI).

Hence their salts should not be prescribed along with alkaline carbonates or hydroxides; e.g. acetate of morphine with bicarbonate of sodium or potassium; or Liq. strychn. with Sp. ammon. aromat. Even borax partially precipitates morphine, cocain, and codein.

R Cocainæ Hydrochlor., gr. v
 Sodii boratis, gr. ii
 Aquæ dist., ʒi

M. Ft. collyrium.

If boric acid were used instead of borax, no ppn. would occur.

If arsenic and strychnine are combined, use Liq. arsen. hydrochlor.

Morphine is soluble in excess of Liq. potassæ, and quinine in excess of Liq. ammoniæ (Tinct. quin. ammon.).

R	Pot. bicarb.,	3 v
	Liq. strychninæ,	5 iss
	Inf. gent. co.,	ad 5 viij
M.							

The bottle was finished up to the last two doses, and laid aside for a fortnight. A sediment was then noticed in the bottle, and after taking the last dose the patient suffered severely from symptoms of strychnine poisoning.

A lady in Johannesburg died in 1898 as the result of taking a mixture containing Liq. arsenicalis and Liq. strychninæ. The physician who ordered the mixture was indicted for culpable homicide. One of his prescriptions was :—

Liq. arsenicalis,	3i
Liq. strychninæ,	3i
Tr. strophanthi	5 iij
Tr. capsici,	5 i
Aquæ,	ad 3vi

(*Chem. and Druggist*, October 12th, 1898.)

In effervescing mixtures the alkaloidal salt should be added to the *acid* bottle.

(b) Most alkaloids are precipitated by—

(i) Tannic acid (not easily by gallic acid).

R	Quin. sulph.,	gr. xii
	Ac. sulph. arom.,	℥20
	Infus. krameriaæ,	ad 3viii
M.						

Quinine tannate is ppd. by the tannin in the rhatany root.

Acetate and meconate of morphine are precipitated by tannic acid, but not the hydrochlorate or sulphate.

(ii) Tincture of iodine, i.e. I + KI.

R	Quin. sulph.	gr. 24 .
	Ac. nitr. dil.,	q. s.
	Potassii iod.,	3 ii
	Aquæ,	ad 3vi
M.						

The nitric acid liberates I from the KI, and quinine is ppd.

Dilute sulphuric acid might be substituted for the nitric acid.

Iodide of potassium alone slowly precipitates some alkaloids from strong solutions.

R.	Pot. iodidi,	5 iiss
	Ferri et quin. citr.,	5 ij
	Tinet. nucis vom.,	5 ij
	Sp. ammon. arom.,	5ss
	Aquæ,	ad 5viiij
M.						

The quinine will be precipitated in part by the ammonia, and slowly as hydriodide.

(iii) Double iodides, e.g. Donovan's solution (Liq. arsen. et hydr. iod.); Mayer's reagent (potassio-mercuric iodide).

Caffein and theobromin are not thus precipitated.

R	Pot. iodidi,	5 i
	Ac. hydrocy. dil.,	3 ss
	Liq. bismuthi,	5 iij
	Quin. sulph.	gr. xij	
	Ac. hydrobrom.,	5 iss
	Aquæ,	ad 5vi
M.							

Double iodide of bismuth and potassium is formed (Dragendorff's reagent), which precipitates the quinine.

(iv) **Pieric acid.** This furnishes a convenient test for quinine in the urine. The precipitate is distinguished from albumen by its complete solution when heated, and reprecipitation upon cooling.

(c) Caustic alkalies decompose the solanaceous alkaloids (atropin : hyoscyamin) and impair or destroy their therapeutic efficacy ; also cocain.

A common error, and one of long standing, is the combination of Liq. potassæ with Tinct. or Succus hyoseyami.

(d) Many other salts of alkaloids are sparingly soluble, e.g. quinine acetate, benzoate, borate, citrate, hydriodide, hydrobromide, and salicylate.

R.	Ferri et quin. citr.,	℥ij
	Pot. citratis,	℥ij
	Ac. citrici,	℥i
	Aquæ,	ad ℥vi
M.						

In a few hours nearly all the quinine was preecipitated as acid citrate in large crystals, and it was impossible to administer the medicine.

R	Quin. sulph.,	gr. x
	Pot. acet.,	gr. xx
	Ac. sulph. dil.,	℥v
	Ac. cinnam.,	ad ʒvi

M.

Mixed in any order a voluminous preecipitate of quinine acetate is thrown down.

A lady lost her life by taking a mixture containing strychnine and bromide of potassium. The last dose contained nearly all the strychnine.

Alkaline salicylates or benzoates and quinine solutions form a voluminous preecipitate of quinine salicylate, e.g. :

Quin. sulph.,	grs. xx
Sod. salicyl.,	ʒ iss
Ac. sulph. dil.,	ʒ i
Aq. pimentæ,	ad ʒviiij

M.

(c) Most of the incompatibilities of alkaloids can be overcome or prevented by dilute HCl, or by alcohol in the proportion of 12 to 40 per cent. of the solution, because alkaloidal salts are usually soluble in alcohol.

In view of the above statements the practical rule emerges :—

All poisonous alkaloids should, so far as possible, be prescribed in simple solution, and not in too concentrated a state.

A woman, aged 57, took the last dose of a mixture containing Liq. strychn. and Liq. bismuthi with Sp. ammon. aromat. In ten minutes she was seized with tonic spasms, involving the face, neck, and body, and was dangerously ill for five hours (*Pharm. Jour.* March 25, 1893).

In especial, morphine and strychnine should not be prescribed in solution along with large quantities of an iodide, bromide, or chloride.

Liq. hydrarg. perchlor. alone *slowly* precipitates strychnine from Liq. strychninæ in delicate acicular crystals: also quinine.

Ac. hydrocyan. dil., or even Aqua laurocerasi, may from solutions of morphine slowly precipitate insoluble morphine cyanide.

A few additional examples of unsuitable or dangerous alkaloidal prescriptions are appended in illustration of the foregoing remarks:—

R	Tinct. guaiaci ammon.,	.	.	.	3 ij
	Mucil. acaciæ,	.	.	.	3 ij
	Quin. sulph.,	.	.	.	gr. viij
	Ac. sulph. dil.,	.	.	.	3 iv
	Pot. bicarb.,	.	.	.	3 i
	Aquæ,	.	.	.	ad 3 iv

M.

An utterly hopeless jumble.

R	Liq. strychn. hydr.,	.	.	.	℥ 100
	Liq. arsenicalis,	.	.	.	℥ 70
	Liq. potassæ,	.	.	.	3 ij
	Aquæ,	.	.	.	ad 3 iij

M.

Quite hopeless.

R	Pot. iodidi,	.	.	.	3 iss
	Liq. strychn.,	.	.	.	3 iss
	Aq. menth. pip.,	.	.	.	ad 3 ij

M.

After twelve hours crystals of hydriodide of strychnine are deposited.

R	Quin. sulph.,	.	.	.	℥ i
	Ac. citrici,	.	.	.	3 iiss
	Syr. ferri iod.,	.	.	.	3 i
	Potass. iod.,	.	.	.	3 i
	Tinct. iodi,	.	.	.	3 iss
	Aquæ,	.	.	.	ad 3 iij

M.

Wrong from more than one point of view.

R	Pot. brom.,	gr. 100
	Pot. bicarb.,	gr. 80
	Quin. sulph.,	gr. 20
	Syr. zingib.,	5 vi
	Aq. menth. pip.,	ad 3viiij

M.

This mixture cannot be dispensed clear.

R	Spir. amm. arom.,	3 vi
	Pot. brom.,	3 ij
	Ferri et quin. citr.,	3 i
	Aquæ,	ad 3vj

M.

The quinine separates as a sticky precipitate.

R	Morph. sulph.,	gr. i
	Pot. bicarb.,	gr. 90
	Aquæ,	ad 3ij

M.

3 i with 3 ss lemon juice.

The morphine is precipitated by the carbonate, and if the bottle had not been shaken before mixing with the lemon juice, the last dose would have contained nearly all the morphine.

EXPLOSIVE AND INFLAMMABLE COMPOUNDS.

Many dangerous and some fatal accidents have happened through carelessness or ignorance of first principles; and I propose now to adduce the more important examples which have occurred in practice.

An explosion may be defined as a sudden and stormy decomposition, attended with noise, and frequently with flame. It is evidently a non-reversible action.

Danger may arise from dealing with either—

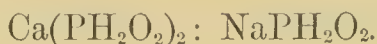
(a) Unstable single molecules.

(b) Processes of rapid and violent chemical reaction between two or more substances.

1. **Unstable Molecule**, i.e. one containing a store of energy in a

condition of stress. This energy is liable to be suddenly liberated, with evolution of much heat:

(i) Hypophosphites of calcium and sodium:—



These salts are liable to explode when simply heated or triturated. A druggist who was engaged in drying some calcium hypophosphite over a sand-bath was killed by the explosion.

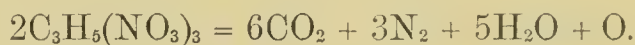
Calcis hypophosph.,	3 ss
Potass. chlorat.	3 ss
M. Ft. pulv. vi. One three times a day.					

When separately powdered and carefully mixed, they were being removed from a glass mortar by a metal spatula, when they suddenly exploded and half stunned the dispenser, blowing off some of his eyebrows and eyelashes (*Ph. Journ.* 3rd Ser., XI. 506).

(ii) Pieric acid and picrates. “Lyddite” is a mixture of pieric acid and gun-cotton.

(iii) Nitro-glycerine (trinitrine).

May explode when shaken or agitated. The Liq. trinitrini B. P., when diluted with water, and let stand, deposits a liquid of oily consistence, one drop of which, absorbed by paper and struck with a hammer on a hard surface, explodes.



“Cordite” is a mixture of trinitrin and gun-cotton.

(iv) Erythrol tetranitrate.

An accident by which a chemist lost his life happened at a tabloid factory in Deptford in 1897. He was engaged mixing tetranitrate of erythrol with finely powdered lactose in a mortar, when an explosion occurred.

A medical man was sent a sample specimen of the same drug. He carelessly threw the bottle containing it into the waste-basket. Next morning the basket was emptied into a dust-pan containing hot ashes. An explosion ensued; the cook was partially stunned,

and received about two dozen small wounds on the hands, arms, and face.

Mannitol hexanitrate explodes violently on being struck with a hammer, or when suddenly heated.

(v) Iodide of nitrogen.

The chemical nature of this compound has been already explained. (p. 18).

It is extraordinary that combinations of Liq. ammoniæ and Tinct. iodi or Liq. ammoniæ with Tinct. iodi and collodion have been recommended as safe for external use, for serious accidents have occurred (Kobert).

II. **Rapid chemical action**, i.e. oxidation or reduction.

This mode of action is naturally observed chiefly in connexion with compounds rich in disposable oxygen; e.g. chlorates, iodates, nitrates, chromates, permanganates, and peroxides.

(a) *In the dry state*—

It is dangerous to triturate potassium chlorate or nitrate with—

(i) Free sulphur, or Pulv. glycyrrh. co. (contains 1 in 12 of sulphur);

(ii) Antimonious sulphide;*

(iii) Finely divided carbon, e.g. in dentrifices;

(iv) Tannin, e.g. catechu.

A mixture of Pot. chlorate, $\bar{3}$ iss, with $\bar{5}$ iss of tannic acid, was rubbed in a new Wedgwood mortar with a rough surface. A violent explosion occurred.

(v) Sugar: Saccharin.

(vi) Hypophosphites. This is very dangerous.

A young pupil rubbed up a mixture of $2\frac{1}{4}$ parts of hypophosphite of calcium, $3\frac{3}{4}$ parts of potassium chlorate, and $\frac{1}{3}$ part of lactate

* The following prescription was presented at a pharmacy in New York:—

Lactis sulphuris,	gr. iij
Antimon. sulph. aurant.,	gr. iij
Zinci valerian.,	gr. i
Potassæ chlor.,	gr. ij. Ft. pulvis.

This cannot be dispensed without an explosion.

of iron. Suddenly the whole mixture took fire, and there was a violent detonation. The young man received such severe burns that his life was endangered.

(vii) Mercuric oxide detonates if rubbed up with iodol.

(b) *In the liquid or moist condition.*

(i) Nitric acid acts violently upon phenol, creosote, and on some volatile oils, e.g. *Oleum terebinthinæ*.

Sawdust has been set on fire by spilling strong nitric acid upon it.

A mixture of nitric acid, hydrochloric acid, and *Tinct. nucis vom.* exploded after some hours (Kobert).

(ii) Chromic acid, CrO_3 , if concentrated, will set fire to glycerine or alcohol.

Such a prescription as this should not be dispensed:—

Ac. chromici,	3 ss
Glycerine,	3 iv
For external use.*						

or Ac. chromic., glycerine, alcohol, equal parts.

(iii) Potassium permanganate can likewise ignite glycerine or alcohol, and detonates when rubbed up with *Confect. rosæ*.

Ext. nuc. vom.,	gr. $\frac{1}{6}$
Ext. aloes aq.,	gr. 1
Pot. permangan.,	gr. 1

The pill mass, when triturated in a mortar, exploded.

An unlucky apothecary attempted to dispense the following formula:—

Pot. permangan.,	}	.	.	.	āā 10 parts
Alcohol,	}	.	.	.	
Distilled water,	15 ,,

Scarcely had the bottle been corked when an explosion took place, and the boiling liquid spurted into the face of the surprised pharmacist. He nearly lost the sight of one eye, and was disabled from work for more than a month.

* A dispenser dissolved the chromic acid in a little water, added the glycerine, and shook up the mixture. Explosion ensued and scattered the contents of the flask.

(iv) Iodine reacts violently upon, and may inflame, some volatile oils, e.g. Ol. terebinth. and Ol. limonis.

A medical man set about manufacturing terebene by acting upon oil of turpentine with pure sulphuric acid. An explosion followed and burnt his clothes. Worse would have happened but that he had taken care to envelop the bottle in a towel.

(v) Oxide of silver, freshly precipitated, develops much heat when rubbed up with creosote, confection of roses, or extract of gentian. Occasionally pills containing the oxide have exploded several hours after dispensing. Silver oxide also forms a very explosive compound with Liq. ammoniæ (Fulminating silver; p. 18).

(vi) Potassium chlorate + Tinct. ferri perchlor. + glycerine, when warm is liable to explode.

This event happened in the pocket of a patient who carried a bottle containing this mixture.

Another time a similar mixture exploded under the influence of the solar rays and set fire to the house.



A curious accident happened in London. A man who was packing capsules of amyl nitrite broke some of them by chance, and the wrapping wool, soaked with the liquid, was thrown out of the window. It happened to fall through a grating beneath which was an open barrel containing chlorate of potassium, which, on contact with the amyl nitrite, blazed up, and nearly set fire to the building.

(vii) Peroxide of sodium (Na_2O_2).

This substance, a light yellow powder, is now an article of commerce, and is prepared on the large scale by the action of air upon metallic sodium at 300° . It is used for bleaching.

When added to water, it develops much heat and liberates oxygen:—



This reaction has been utilized in the study of the respiratory function in animals in a confined space. The products, viz. oxygen

and caustic soda, are precisely those necessary to absorb CO_2 , and replace it by oxygen. Calcium peroxide (CaO_2) has been suggested by Nencki and Zalesky as an intestinal antiseptic.

If some of the freshly made peroxide be wrapped in muslin, or in cotton wool, and water be dropped upon it, the whole bursts into flame.

The peroxide at once sets glycerine on fire, and if added to commercial formalin a very violent explosion occurs.

This latter experiment should be performed only with small quantities.

A bandage which had been soaked in a solution of peroxide of hydrogen ignited when dry.



APPENDIX.

Changes which drugs and preparations may undergo by time and exposure, i.e., by external agencies, or by internal molecular changes.

I.—Radiant Energy.

Radiant energy can transform itself into almost every other form of energy, most easily and completely into heat. We do not now trouble to distinguish between the effects of radiant heat, light, and chemical influence. The chemical action of light represents usually but a small fraction of its total energy.

The light action is partly *oxidizing*, and partly *reducing*, but these are only relative terms. Light may favour chemical decomposition, e.g., grey powder and iodoform, mixed together, slowly become salmon-coloured, and some of the irritant and poisonous HgI_2 is formed. Phenol often turns red on keeping: no harm.

Santonin preserves its pure whiteness indefinitely in the dark. Exposure to light soon turns it bright yellow. Its dose and therapeutic properties are not affected thereby.

Apomorphine hydrochloride, white when freshly prepared, slowly becomes green even in the solid state; and an aqueous solution quickly darkens and becomes black. Such a discoloured solution is unfit for use. Salts of physostigmin acquire a red colour by exposure. Quin. Sulph., salts of morphine, especially the acetate, and calomel, darken on exposure to light.

Coloured tinctures and other preparations are frequently bleached by long exposure to light, e.g., Fowler's solution.

II.—Absorption or Extrication of Water.

Some solid substances greedily absorb water and become moist or even liquid, and are said to be *deliquescent* or *hygroscopic*, e.g.

caustic potash and soda, calcium chloride, potassium acetate and carbonate, zinc chloride. Such bodies are evidently unsuited for prescription in powder form.

Some liquids, e.g., oil of vitriol and strong alcohol, are hygroscopic; and it is very difficult to prepare alcohol stronger than 99 per cent. Owing to its dehydrating action, strong alcohol throws gum out of solution from solution, and certain salts (sulphates, phosphates), out of watery solution, e.g. from urine.

Some salts, rich in water of crystallization, slowly part with some or all of this water, and tumble into powder. They are said to be *efflorescent*, e.g., “Washing Soda” (Sod. Carb.), borax, alum. Efflorescence may be regarded as a “dissociation evaporation.”

III.—Absorption or loss of CO_2 .

The caustic alkalies, lime-water, lead acetates, especially the subacetate, absorb CO_2 from the atmosphere. Hence, the white ppt. of oxycarbonate often noticed in “lead lotion,” and of calcium carbonate in lime-water.

“Fluid Magnesia” (Liq. magnes. carb.) loses CO_2 , and deposits a crystalline ppt. of hydrous MgCO_3 .

IV.—Absorption of Oxygen.

Certain lower oxides readily absorb oxygen from the air, or other source, and pass into higher oxides. E.g., sulphurous into sulphuric acid, nitrous acid and nitrites into nitrates; ferrous into ferric compounds. Sugar retards this process, e.g., Syr. ferri iodidi, and Syr. ferri phosph.

Volatile (essential) oils and oleo-resins slowly absorb oxygen, darken in colour, lose some of their aroma, thicken, and may ultimately form resins; e.g., Ol. terebinth; Terebinth. canad. Resins in plants are probably formed in this fashion. Aldehydic volatile oils, e.g., oil of cinnamon and oil of bitter almonds, oxidize into the corresponding crystalline acids, cinnamic and benzoic acids, respectively.

V.—Reduction Processes.

Pure silver nitrate is not acted on by light alone, but in presence of organic matter it is slowly reduced even in the dark, and exposure to light simply accelerates change (photography ; argyria). Potassium permanganate is quickly reduced by organic matter, and hence its action as a deodorizer. Condyl's fluid stains the skin brown (MnO_2), and the deposit is easily removed by oxalic acid (or "salt of lemon"). "Reducing agents" often have a powerful irritant action on the skin, e.g., Resorcin, Pyrogallol. As we have already seen, many explosive or inflammable mixtures arise from rapid oxidation or reduction.

VI.—Changes due to Parasites.

Many drugs and preparations are liable to deterioration from such causes; mainly from growth and development of minute fungi and of algæ.

Ergot, itself the product of a fungus parasitic on rye-grains, is very prone to subsequent vitiation, bacterial and otherwise, and accordingly old specimens are unreliable.

Most watery solutions of vegetable drugs, e.g., infusions, decoctions, liquid extracts, and succi, are not suited for long keeping, owing to the development of moulds and other extraneous growths. Alkaloidal solutions, if long made, are liable to development of fungi or algæ.

